REMARKS

Applicants respectfully request reconsideration of the application, as amended, in view of the following remarks.

Claim 15 has been canceled. The limitations of Claim 15 have been incorporated in Claim 10.

Amended Claim 10 is directed to an oil-based transdermal absorption preparation. No new matter is believed to have been added by entry of this amendment. Entry and favorable reconsideration are respectfully requested.

Upon entry of this amendment Claims 10-14 and 16-18 will now be active in this application.

Prior art references applied in the Office Action:

Applicants wish to draw the Examiner's attention to MPEP 706.02 II, which requires the Examiner to provide a full translation for any references she relies on in a rejection.. It is improper to simply rely on an abstract:

> "Citation of and reliance upon an abstract without citation of and reliance upon the underlying scientific document is generally inappropriate where both the abstract and the underlying document are prior art. See *Ex parte Jones,* 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) (unpublished).To determine whether both the abstract and the underlying document are prior art, a copy of the underlying document must be obtained and analyzed. If the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying upon in support of the rejection. The record must also be clear as to whether the examiner is relying upon the abstract or the full text document to support a rejection.

The objection of Claim 16 is obviated by the Amendment of Claim 16.

The rejections of the claims under 35 U.S.C. § 103(a) over El Khoury in view of Higo et al, Narui et al in view of Higo et al, Hirabayashi et al in view of Higo et al, Yanagawa et al in view of Higo et al, and Narui et al or Hirabayashi et al or Yanagawa et al in view of Higo et al and further in view of Cho et al are respectfully traversed.

An object of the present invention is to overcome the above problems and provide a transdermal absorption promotion composition and transdermal absorption preparation that can not only exhibit an excellent transdermal absorption promotion effect, but also exhibit superior skin-permeability, even if a drug having a relatively high lipophilic property and poor transdermal absorbability is used, exhibit a favorable feeling of use, and are safe and stable.

See the specification at page 2, lines 13-18.

The present inventors have conducted extensive studies to achieve the above object and found that a transdermal absorption promotion composition containing propylene glycol, a polyol fatty acid ester, and a lauromacrogol remarkably increases permeability of drugs through the skin. The present inventors have further found that the transdermal absorption preparation prepared by adding a drug to the transdermal absorption promotion composition exhibits remarkably excellent transdermal absorptivity of the drug, a favorable feeling of use, and stability, and imparts only slight stimulation to the skin. These findings have led to the completion of the present invention.

See the specification at page 2, line 21 to page 3, line 2.

Amended Claim 10 relates to an oil-based transdermal absorption preparation, comprising:

(a) propylene glycol,

(b) a polyol fatty acid ester,

(c) lauromacrogol which is selected from the group consisting of lauryl ethers with 2 to 25 mol ethylene oxide addition, and

(d) loperamide hydrochloride or lidocaine;

wherein said oil-based transdermal absorption preparation is an oily ointment or oily cream preparation.

In addition, Applicants wish to draw the Examiners' attention to Figures 1 and 2 which show data from the Examples and Comparative Examples of the specification.

The relationship between the amounts of accumulated loperamide hydrochloride extracted from solutions of Example 1 and Comparative Examples 1-3 that penetrated the rat skin and the time elapsed is shown in FIG. 1. As is clear from FIG. 1, the solution of Example 1 which contains propylene glycol, propylene glycol monocaprylate, and polyoxyethylene (2) lauryl ether was confirmed to exhibit higher skin permeability than the solution of Comparative Example 1 containing only propylene glycol, the solution of Comparative Example 2 containing propylene glycol and propylene glycol monocaprylate, and the solution of Comparative Example 3 containing propylene glycol and polyoxyethylene (2) lauryl ether.

See page 9, lines 18-26 of the specification.

The relationship between the amounts of accumulated drug that penetrated the rat skin from the ointments of Example 2 and Comparative Examples 4-6 and the time elapsed is shown in FIG. 2. As clear from FIG. 2, the solution of Example 2 which contains propylene

glycol, propylene glycol monocaprylate, and polyoxyethylene (2) lauryl ether was confirmed to exhibit higher skin permeability than the solution of Comparative Example 4 containing only propylene glycol, the solution of Comparative Example 5 containing propylene glycol and propylene glycol monocaprylate, and the solution of Comparative Example 6 containing propylene glycol and polyoxyethylene (2) lauryl ether.

See page 11, lines 12-20 of the specification.

The transdermal absorption promotion composition of the present invention and the transdermal absorption preparation containing the composition and a drug component not only exhibit a transdermal absorption promotion effect, but also exhibit superior skin-permeability, even if a drug having a relatively high lipophilic property and poor transdermal absorbability is used, exhibit a favorable feeling of use, and are safe and stable.

Therefore, the transdermal absorption promotion composition of the present invention and the transdermal absorption preparation containing the composition and a drug component are useful for transdermally administering various drugs to patients.

See page 11, line 23 to page 12, line 4 of the specification.

El Khoury in view of Higo et al, Narui et al in view of Higo et al, Hirabayashi et al in view of Higo et al, Yanagawa et al in view of Higo et al, and Narui et al or Hirabayashi et al or Yanagawa et al in view of Higo et al and further in view of Cho et al do not render obvious the present invention as claimed.

El Khoury discloses the components (a) to (c) of the present invention solely as examples of a transdermal absorption enhancing agent for use in a transdermal absorption preparation. There is no disclosure or suggestion of a combined use of these components.

There is no disclosure of suggestion to combine (a) to (c) with (d). There is no expectation of the properties of a combination of (a) to (c) with (d). However, in the present invention, a significant synergistic enhancing effect can be expected with the combined use of components (a) to (c) and drug (d).

Similarly, Yanagawa et al do not disclose the use of a component (d) in combination with components (a) to (c).

Narui et al. and Hirabayashi et al. disclose a composition comprising the components (a) to (c) of the present invention and water. However, the composition is water-based, and not oil-based as the present invention. Further, the enhanced transdermal absorbency of the present invention is not predictable from the disclosures of the references. In addition, the references do not mention the components (a) to (c) as being essential features.

Higo et al. solely suggest use of a drug for transdermal absorption.

Cho was only cited for disclosing surfactants for transdermal compositions.

As explained above, El Khoury does not show any Examples of combined use of the components and further, the composition of Narui et al. and Hirabayashi et al. is water-based whereas the preparation of the present invention is oil-based.

Thus, El Khoury in view of Higo et al, Narui et al in view of Higo et al, Hirabayashi et al in view of Higo et al, Yanagawa et al in view of Higo et al, and Narui et al or Hirabayashi et al or Yanagawa et al in view of Higo et al and further in view of Cho et al do not render obvious the present invention as claimed.

Therefore, the rejections of the claims under 35 U.S.C. § 103(a) over El Khoury in view of Higo et al, Narui et al in view of Higo et al, Hirabayashi et al in view of Higo et al, Yanagawa et al in view of Higo et al, and Narui et al or Hirabayashi et al or Yanagawa et al in view of Higo et al and further in view of Cho et al are believed to be unsustainable as the

present invention is neither anticipated nor obvious and withdrawal of these rejections is respectfully requested.

This application presents allowable subject matter, and the Examiner is kindly requested to pass it to issue. Should the Examiner have any questions regarding the claims or otherwise wish to discuss this case, he is kindly invited to contact Applicants' below-signed representative, who would be happy to provide any assistance deemed necessary in speeding this application to allowance.

Respectfully submitted,

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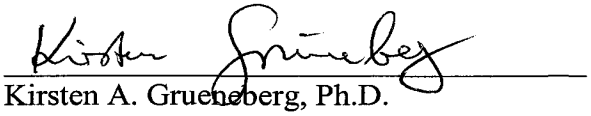

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